

# Rhabdomyosarcoma of the clitoris

Youssef Al-Tonbary,<sup>a</sup> Khalid Zalata,<sup>b</sup> Mohamed Sarhan,<sup>a</sup> Rasha El-Ashery,<sup>a</sup> Ashraf Fouda<sup>a</sup>

From the <sup>a</sup>Haematology/Oncology Unit and <sup>b</sup>Pathology Department, Mansoura University Children's Hospital, Mansoura, Egypt

Correspondence and reprints: Prof. Youssef Al-Tonbary · Hematology/Oncology Unit, Mansoura University Children's Hospital Mansoura, Egypt · T: +2012-316-5302 F: +2050-226-2307 · ytonbary@gmail.com · Accepted for publication March 2008

Hematol Oncol Stem Cell Ther 2008; 1(2); 133-135

**S**oft tissue sarcomas are the sixth most common malignancy in childhood and rhabdomyosarcomas constitute about 50% of soft tissue sarcomas. This tumor accounts for 10% to 15% of solid malignant tumors and 6% of all malignancies in children under 15 years of age. In the United States, the male-to-female ratio is 1.5:1, and the tumor is twice as common in whites as in African-Americans. Approximately 250 new cases are diagnosed every year.<sup>1</sup>

Rhabdomyosarcoma is a malignant tumor of striated muscle but, because of its mesenchymal origin, can originate in tissue that does not normally contain striated muscle (for example, the ureter). There is a bimodal distribution of rhabdomyosarcoma with peaks between 2 and 4 years of age and 12 and 16 years of age. Nearly 80% of rhabdomyosarcoma is diagnosed by the age of 14 years. The most common primary sites for rhabdomyosarcomas include the head and neck, the genitourinary tract, and extremities. However, primary sites with a favorable prognosis include the orbit and nonparameningeal, head and neck, paratestis, the vagina, and the biliary tract.<sup>2,3</sup>

## CASE

A 3-year-old female had a 6-month history of genital swelling. Gynecological examination revealed that she had clitoral swelling. Ultrasound revealed a cystic mass, which was mostly a clitoral cyst. CT of abdomen and chest were free, while a CT of the pelvis showed clitoral soft tissue swelling that was 2×3 centimeters in diameter for clinical and pathological evaluation. Alpha-fetoprotein was 1.1 ng/mL (normal range, 0-10 ng/mL). She had been misdiagnosed as having congenital adrenal hyperplasia presenting with clitoromegaly, but specific tests (serum cortisol, dehydroepiandrosterone sulfate and testosterone) were normal. Surgical resection of the clitoris was done, but a pathological examination was neglected.

The patient presented to us 4 months later with a recurrent mass at the mons pubis (Figure 1). The mass was hard and about 3×4 centimeters in diameter, fixed to the underlying structures and not the skin, but the

overlying skin was hyperemic with dilated vessels, and no enlarged inguinal lymph nodes. Vaginal inspection was free, and the rectal examination was also free. A CT of the pelvis showed hypertrophy of the soft tissue of the clitoris (Figure 2).

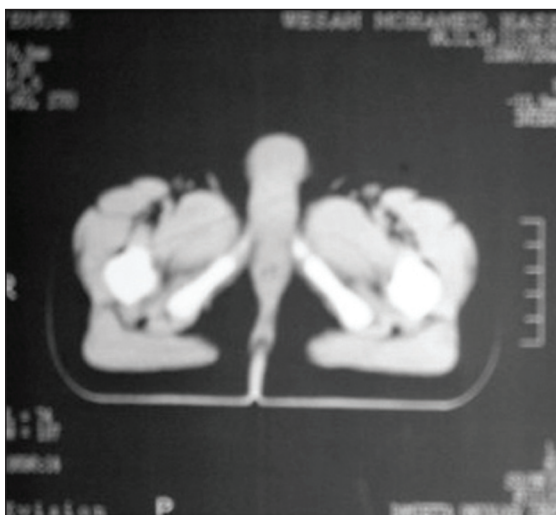
A biopsy was taken from the mass (grayish white, 2×3.5×2 centimeters) and hematoxylin and eosin stain revealed highly pleomorphic small cells with small rounded nuclei and large spindle-shaped cells with vesicular nuclei and acidophilic cytoplasm. The tumor cells were disposed in a rich collagenous fibrous stroma (malignant rounded cell tumor, mostly embryonal rhabdomyosarcoma) (Figure 3). A desmin stain was positive. Complete surgical excision of the mass was done and the patient received chemotherapy for rhabdomyosarcoma (VAC protocol scheduled for 43 weeks: vincristine, 1.5mg/m<sup>2</sup> IV; actinomycin D, 0.015mg/kgm/day IV for 5 days; cyclophosphamide, 2.2gm/m<sup>2</sup> IV with mesna). She also received pelvic radiation therapy for 5 weeks. After 10 months, follow up MRI revealed the presence of a soft tissue mass (3×4×4.5 centimeters) at the site of the previous operation with invasion to the skin only and no invasion to underlying bone or interior of the pelvis. The patient was surgically operated on again for treatment of this local recurrence.

## DISCUSSION

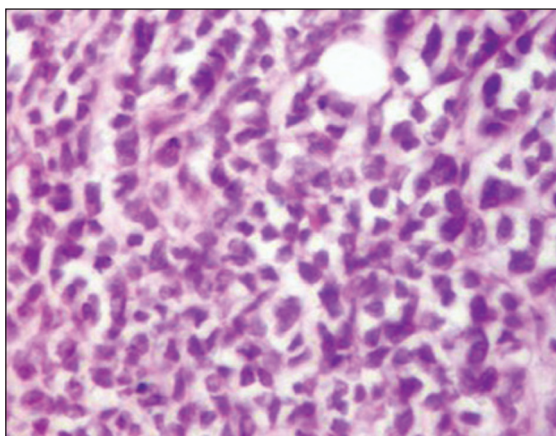
Clitoromegaly can be either congenital or acquired. The congenital forms are caused by hormonal disturbances or intersex states. Usually they are obvious at birth. When the clitoromegaly develops later, the underlying etiology should be explored and acquired causes should also be considered. These acquired forms of clitoromegaly are either hormonal or non-hormonal. In the hormonal causes, an androgen excess is the main contributing factor for the clitoral enlargement. Three groups are generally distinguished: endocrinopathies, masculinizing tumors, or self-injection of long-acting synthetic androgens,<sup>4</sup> but clitoral tumors should be considered in the differential diagnosis. The clitoris can be involved in a variety of benign and malignant



**Figure 1.** Clitoral mass after recurrence.



**Figure 2.** CT of the pelvis showing hypertrophy of the soft tissue of the clitoris.



**Figure 3.** Hematoxylin and eosin stain of the clitoral biopsy showing a malignant rounded cell tumor.

neoplasms. Among the multiple reports of neoplasms involving the clitoris are angiokeratoma,<sup>5,6</sup> hemangioma,<sup>7</sup> neurotumors associated with neurofibromatosis,<sup>8</sup> keratoacanthoma<sup>9</sup> and lymphoma.<sup>10</sup> In adults, the most common malignancies involve squamous cell carcinomas of the vulva that invade the corporal bodies.<sup>11,12</sup> The clitoris is rarely a metastatic site and equally as rare is a primary sarcoma of the vulva that may extend to the clitoris.<sup>13-15</sup>

The most common sites of presentation of rhabdomyosarcoma are genitourinary (29%), parameningeal (24%), the extremities (15%), retroperitoneal (13%), orbit (8%), other head and neck (7%), and miscellaneous sites (4%). Most often, rhabdomyosarcoma presents as a rapidly enlarging mass lesion, although often the manifestations of tumor growth depend on the primary tumor site.<sup>16</sup> The genitourinary sites of this lesion in younger females are primarily vaginal, cervical, and uterine, with occasional tumor extension to involve the urethra and labia. A lesion that originates superficial to the introitus is rare, although a few cases of vulvar rhabdomyosarcoma exist.<sup>17,18</sup>

Rhabdomyosarcomas arise in primitive fetal mesenchyme even at sites that do not contain skeletal muscle. It also manifests immunohistochemical expression of myosin, actin, desmin, myoglobin and Z-band protein. Histologically, there are four subtypes: embryonal, alveolar, botryoid and pleomorphic.<sup>19</sup> The embryonal subtype represents about 54% of rhabdomyosarcomas. This subtype usually occurs before 8 years of age and accounts for 80% of genitourinary tumors, 60% of head and neck tumors and 50% of tumors at other sites. The tumor is poorly circumscribed, soft and whitish in color. Morphologically, it resembles the developing skeletal muscle of the 7-10 week old fetus. Rhabdomyoblasts can take several characteristic morphologic appearances.<sup>20</sup>

All patients with rhabdomyosarcoma are presumed to have micrometastatic disease at diagnosis, and thus successful treatment requires achievement of both local and systemic control of disease. Systemic control is achieved by chemotherapy even for patients with localized disease to eradicate the micrometastasis. The chemotherapy regimens used include a combination of the effective agents in rhabdomyosarcoma, which are cyclophosphamide, ifosfamide, melphalan, actinomycin D, adriamycin, cisplatin, carboplatin, vincristine and etoposide. Local control is accomplished by complete surgical excision and/or local irradiation.<sup>21</sup>

Clitoral rhabdomyosarcoma in children is a very rare tumor, reported only in few cases.<sup>22-24</sup> It may have a poor prognosis and may be resistant to treatment due to delay

in diagnosis and treatment. Clitoral tumors, although very rare, should be considered in the differential diagnosis of any clitoral enlargement, especially with normal hormonal studies for exclusion of adrenogenital syndromes.

## REFERENCES

1. O'Neill JA Jr, Grosfeld JL, Fonkalsrud EW, Coran AG, Caldamone AA. Rhabdomyosarcoma: In O'Neill JA Jr, Grosfeld JL, Fonkalsrud EW, Coran AG, Caldamone AA, eds: *Principles of Pediatric Surgery*. 2nd edn. St. Louis, MO 2003, Mosby, P. 229-238.
2. Crist WM, Garnsey L, Beltangady MS, et al: Prognosis in children with rhabdomyosarcoma: a report of the intergroup rhabdomyosarcoma studies I and II. Intergroup Rhabdomyosarcoma Committee. *J Clin Oncol* 1990;8:443-452.
3. Spunt SL, Lobe TE, Pappo AS, et al: Aggressive surgery is unwarranted for biliary tract rhabdomyosarcoma. *J Pediatr Surg* 2000;35: 309-316.
4. Guelinckx PJ, Sinsel NK: An unusual case of clitoral enlargement: its differential diagnosis and surgical management. *Acta Chir Belg*. 2002;102(3):192-195.
5. McNeely TB: Angiokeratoma of the clitoris. *Arch Pathol Lab Med* 1992; 116:880-881.
6. Yamazaki M, Hiruma M, Irie H, Ishibashi A: Angiokeratoma of the clitoris: a subtype of angiokeratoma vulvae. *J Dermatol*. 1992;19(9):553-555.
7. Bouchard S, Yazbeck S, Lallier M: Perineal hemangioma, anorectal malformation, and genital anomaly: a new association? *J Pediatr Surg*. 1999;34(7):1133-1135.
8. Kantarci M, Alper F, Aliagaoglu C, Yildirim U, Onbas O, Sivri F: Neurofibromatosis of the labium majus and clitoris: an unusual image reminiscent of ambiguous genitalia. *Acta Obstet Gynecol Scand*. 2005;84(1):96-98.
9. Nascimento MC, Cominos D, Davies NJ, Obermair A: Vulval Keratoacanthoma: a case report. *Gynecol Oncol*. 2005;97(2):674-676.
10. Kosari F, Daneshbod Y, Parwaresch R, Krams M, Wacker HH: Lymphomas of the female genital tract: a study of 186 cases and review of the literature. *Am J Surg Pathol*. 2005;29(11):1512-1520.
11. Hanna SJ, Kaiser L, Muneer A, Nottingham JF, Kunkler RB: Squamous cell carcinoma of the bladder presenting as vulvitis and cliteromegaly. *Gynecol Oncol*. 2004;95(3):722-723.
12. Semczuk A, Skomra D, Jankiewicz K, Adamiak A, Korobowicz E, Rechberger T: The immunohistochemical profile of the primary and metastatic carcinoma of the clitoris: a case report. *Arch Gynecol Obstet*. 2005;273(3):187-91.
13. Piver MS, Tsukada Y: Epithelioid sarcoma of the vulva. *Obstet Gynecol* 1972; 40:339-342.
14. Langenstroer P, Romanas M, Damjanov I: Clitoromegaly caused by metastatic carcinosarcoma of the urinary bladder. *Arch Pathol Lab Med*. 2003;127(4):505.
15. Androulaki A, Papatomas TG, Alexandrou P, Lazaris AC: Metastatic low-grade endometrial stromal sarcoma of clitoris: report of a case. *Int J Gynecol Cancer*. 2007;17(1):290-293.
16. Breitfeld PP, Meyer WH: Rhabdomyosarcoma: new windows of opportunity. *Oncologist*. 2005;10(7):518-527.
17. Hays DM, Shimada H, Raney RB Jr., Tefft M, Newton W, Crist WM, et al: Clinical staging and treatment results in rhabdomyosarcoma of the female genital tract among children and adolescents. *Cancer* 1988; 61:1893-1903.
18. Donaldson SS: Rhabdomyosarcoma: contemporary status and future directions. *Arch Surg* 1989; 124:1015-1020.
19. Andrea Stuart and Jayant Radhakrishnan. Rhabdomyosarcoma Indian J Pediatr 2004; 71 (4) : 331-337.
20. Wiener ES. Rhabdomyosarcoma. In O'Neill JA Jr, Rowe MI, Grosfeld JL, Fonkalsrud EW, Coran AG, eds. *Pediatric Surgery*, 5th edn. St. Louis, MO, 1998, Mosby, pp 431-445.
21. Breitfeld PP, Meyer WH. Rhabdomyosarcoma: new windows of opportunity. *Oncologist*. 2005; 10(7):518-527.
22. Nag S, Grecula J, Ruymann FB: Aggressive chemotherapy, organ-preserving surgery, and high-dose-rate remote brachytherapy in the treatment of rhabdomyosarcoma in infants and young children. *Cancer*. 1993; 72(9):2769-2776.
23. Bond SJ, Seibel N, Kapur S, Newman K D: Rhabdomyosarcoma of the clitoris. *Cancer*. 1994; 73(7):1984-1986.
24. Ghushie ND, Drugas GT. Rhabdomyosarcoma of the clitoris. *Pediatr Radiol*. 2007; 37(11):1179.